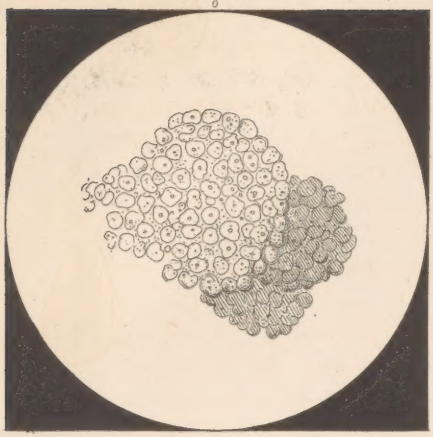
Broca (P.)

Fig 1.



TERMINAL VESICLES OF GLANDS OR GLANDU-LAR CULS-DE-SAC.—MAGNIFIED 270 DIAMETERS.

Fig. 2.

MICROSCOPIC ELEMENTS OF A FIBRO-PLASTIC TUMOUR.—MAGNIFIED 460 DIAMETERS.

Fig 3.

ELEMENTS OF AN EPITHELIAL TUMOUR.—270 DIAMETERS.

Fig. 4.

CANCEROUS ELEMENTS.—MAGNIFIED 460 TIMES.

T. Sinclair's lith, Phila.

Presented by J. J. Woodward

EXPLANATION OF THE PLATE.

FIGURE 1 represents the oval cœcal terminations of the gland tubes, or glandular culs-de-sac, as seen under a magnifying power of 270 diameters, obtained by objective No. 5, ocular No. 1 of Nachet's microscope.

FIGURE 2 represents various fibro-plastic elements as exhibited obj. 7, ocul. 1, micr. Nachet (460 diameters).

a. Fibro-plastic nuclei; *b*. Fibro-plastic cells; *c*. Fibro-plastic fuseform bodies; *d*. Fibro-plastic fibres at different stages of evolution; *e*. Fibro-plastic fibres arranged in fibroid tissue.

FIGURE 3. Epithelial elements. (Obj. 5, oc. 1. micr. Nachet.)

a. Free epithelial nuclei; *b*, *c*, Small epithelial cells. Above the cell *b*, two large superimposed cells are delineated; *d*, *e*. Epithelial cells seen in profile, and irregularly bent.

FIGURE 4 shows the microscopical elements that characterize cancerous tumours. (Obj. 7, oc. 1, micr. Nachet.)

a. Free cancer nuclei; *b*. Small cancer cell; *c*. A larger cell; *d*, A cell with two nuclei; *e*. A mother-cell; *f*. A mother-cell containing a simple nucleus, and a nucleated cell; *g*. A large irregular bifurcated cancer cell.

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ART. I.—*A Classification of Tumours Confounded under the Name of Cancer.* By PAUL BROCA, Agrégé Professor to the Faculty of Paris, Surgeon to the Hospitals, etc. [Translated from the *Moniteur des Hôpitaux*, December, 1854.]

The utility and precision of the information furnished by the microscope is no longer contested. The clinical interpretation of the phenomena revealed by this precious instrument is alone a subject of discussion. We may therefore lay aside the polemical pen, and treat in didactic style of the principal distinctions between morbid growths confounded under the name of cancer, as established by the microscope, and of the history of pseudo-cancerous tumours.

It is very difficult to determine accurately what were included and what excluded from the class of tumours that the classic authors variously denominated cancer, schirrus, carcinoma, fungus, sarcoma, degenerated or malignant growths, etc. The structure of these tumours varied yet more than their names, to the despair of morbid anatomists; and their symptoms varied yet more than their structure, to the confusion of clinical observers. They formed a heterogeneous group, in which the most dissimilar formations were associated; tumours of great density, or of a softness approaching fluidity; semi-transparent tumours

and opaque ones; tumours as black as ink and those of milky whiteness;—a group of such indefinite limits that optimists were enabled to declare that the majority of cancers could be eradicated, while pessimists attributed to the same disease a constant and inevitable fatality.

When the positive science of the nineteenth century came in presence of this antiquated lumber; when Abernethy, Scarpa, Astley Cooper, Laënnec, Bayle, and their compeers, began to look into the subject with care, and compared symptoms with cadaveric lesions, these great observers were sadly perplexed. The anatomo-pathologists, on the one hand, could not comprehend how the same disease should be attended in different cases by such strangely dissimilar lesions, that set at defiance all their established rules. On the other hand, the nosologists demurred at the caprices of a malady, that gave rise to the most antagonistic assertions. Some surgeons, in fact, regarded an operation for cancer as a mere prelude to relapse, while others claimed frequent success for the treatment by the knife. Such testimony was calculated to excite a distrust in observation, and was irreconcilable with uniformity in pathological laws.

Such was the state of science, when Muller began to examine into the microscopical characters of tumours, an idea that was eagerly followed by the entire German school. This was in 1839, just as the Cell Theory had blazed abroad in its brightest effulgence.

The various tumours regarded as appertaining to the class of cancers were soon examined, and pathologists had the satisfaction of finding that, whatever their differences in colour, density, or vascularity, they all contained innumerable microscopic cells. They scarcely paused to enquire if these cells were everywhere alike. Their diversities were assuredly less glaring than those that the naked eye distinguished in schirrus and encephaloid, in colloid and melanosis. There was some cause for satisfaction, indeed. The *pathological cell* was apparently that connecting link uniting the dissimilar types of cancer which had been long sought for in vain. What chemistry had essayed unavailingly, what the scalpel had failed in, the microscope had realized at the very outset! A grand result, surely; and the anatomo-pathologists chanted pæans for it.

But the clinicians were less triumphant. What was it to them that the anatomical unity of cancer was demonstrated, when its symptoms and progress displayed so little uniformity? If the structure of cancerous tumours was identical, the diversities in its results were only the

more unaccountable. It was known that there were mammary tumours, for example, that were quite innocent, and others of most discouraging malignancy; that the *noli me tangere* of the face were less malignant than some other cancerous tumours. If the microscope found cells in all of them, the conclusion seemed inevitable that pathological anatomy was in contradiction with clinical observation.

Such a contradiction really existed. Where the micrographers found unity, the practical surgeon was sure there was diversity. The confusion that resulted may be compared to the state of science in regard to the diseases of the thoracic organs just anterior to the researches of Laënnec.

Such a state of things could not last long. It ceased necessarily when practitioners took pains to study with the microscope, and micrographers made themselves acquainted with diseases; when pathological histology and clinical medicine were no longer regarded as distinct branches of knowledge; when, in a word, the morbid anatomy of the microscope was investigated as Morgagni, Abernethy, and Laënnec had investigated the morbid anatomy of the scalpel.

M. Lebert opened this new field, and was presently followed by those who now constitute the young School of Paris. The enterprize was a difficult one, requiring perseverance and even courage. For it seemed unlikely that two branches of research, like microscopy and clinical observation, that had thus far been pursued separately, could be conjoined without reciprocal modifications. Therefore those who attempted to unite them were exposed to criticism and recrimination. They anticipated this, and were not disappointed. Micrographers considered them clinical students utterly incompetent in matters of microscopy,—clinical observers pronounced them micrographers quite ignorant of clinical medicine,—fogies who were neither clinicians nor micrographers scoffed at them as imprudent and troublesome innovators.

We will not dwell longer on the causes of the revolution which has taken place in the last ten years. We will proceed at once to describe the microscopical elements that characterize the tumours confounded under the name of cancer, and to present drawings of these elements, in order that our description may be more intelligible.

An examination of morbid growths, including a comparison of their appearances before and after removal, enables us to distribute the various tumours, that have long been confounded under the vague and elastic designation of cancer, into four groups.

1. *Partial glandular hypertrophies*, or glandular tumours, in which the microscope discovers only the elements that enter normally into the structure of glands; these elements being unequally hypertrophied.

2. *Fibro-plastic or fibroid tumours*, constituted by elements analogous to the component structures of certain normal tissues, and designated fibro-plastic elements.

3. *Cancroid epithelial tumours*, constituted by elements analogous to those that form the epithelium of normal tegumentary tissues.

4. *Cancerous Tumours*—properly so called, constituted by elements that have no analogy in the economy, to which the name of cancerous elements is legitimately applied.

I.—*Partial glandular hypertrophies* or *adenoid tumours.*—All glands are liable to hypertrophy; all of them possess normally a fundamental part, that is always of the same nature, however manifold its form and connections. This is the *gland-cavity*, which contains the secreted product. This cavity is bounded by a membrane, the internal surface of which is paved with epithelium. In the vascular or closed glands, the gland-cavity is a shut sac; this obtains, for example, in the thyroid, supra-renal capsules, thymus, etc. In the other glands, the gland-cavity communicates directly or indirectly with the excretory duct.

The structure of hypertrophic tumours varies with the normal structure of the hypertrophied organ. A consideration of all the varieties of glandular enlargement would be foreign to our present purpose. We shall therefore confine our attention to hypertrophies of the racemose or acinous glands, such, for example, as the mamma or parotis.

Apart from the vessels and nerves distributed to them, these glands are composed of two parts: 1. Gland-cavities, which here present themselves under the form of little recesses or saccules opening into the branches of the excretory ducts. The membrane that lines these saccules is continuous with the mucous lining of the excretory ducts. In other words, we may describe this anatomical arrangement by saying that the ducts or gland-tubes terminate in cæcal pouches or culs-de-sacs. The membrane lining these vesicular recesses is paved by a layer of nucleolar epithelium, composed exclusively of epithelial nuclei. Each nucleus has a nucleolus, but no enveloping membrane (cell wall) exists around them as in epithelium composed of cells. (*See* PLATE, Fig. 1.) 2. The second characteristic component of these glands is the *fibro-cellular stroma*, which constitutes the skeleton of the organ so to speak.

This substance consists of fibres of cellular tissue of different degrees of density, which surround the glandular lobules, supporting them, and binding them together.

These two elements are found in all glandular hypertrophies.

In *general hypertrophies*, these two elements are developed simultaneously and uniformly. The gland presents nearly the same aspect as in the normal state. No one has confounded this condition with cancer.

In *partial hypertrophies*, on the contrary, the fundamental elements of the gland are unequally developed. When the fibro-cellular tissue chiefly is hypertrophied, the tumour is hard, it creaks under the knife, and has been mistaken for schirrus. When the hypertrophy is confined mainly to the glandular vesicles, the tumour is soft, easily torn or crushed between the fingers. This form of disease has been confounded with encephaloid.

These two varieties of glandular hypertrophy exhibit, under the microscope, a gland structure altogether analogous to what is observed in the normal state. In the first form, there is an abundance of filaments, and the vesicles are not more developed than in their physiological state. In the second form, the fibro-cellular tissue is scanty, while the vesicles are much enlarged; this is all the difference. In both cases, we find the characteristic cæcal terminations throughout the tumour, perfectly distinguished by their rounded form and the regular arrangement of their epithelial elements.

This epithelium is usually altogether *nuclear*, as in the normal state. (*See* Fig. 1.) But it is not uncommon, especially in the second form of hypertrophy to find nuclei of epithelium invested by a cell membrane. In other words, the epithelium sometimes passes from the nuclear to the cellular form. A certain number of *nucleated cells* are perceived in the field of the microscope, under these circumstances, and some careless observers have mistaken these microscopical elements for those of cancer. Such an error will not be committed by any one who studies the *arrangement* of these epithelial cells, and notes their regular juxtaposition in the cavity of the glandular culs-de-sac.

II.—*Fibro-Plastic or fibroid tumours.*—These tumours are composed of elements analogous to those that exist in the cellular tissue in its formative stage. These elements are found in different states of transition, from the globular to the fibrous. (*See* Fig. 2.)

Free fibro-plastic nuclei (Fig. 2, *a.*) are small oval, occasionally round, bodies, presenting an extremely small central functiform nucleolus.

Fibro-plastic cells (*b.*) consist of a nucleus like the free nuclei, and an external membrane investing this nucleus. These cells are long and narrow. Their extremities are pointed.

Fibro-plastic fusiform bodies (*c.*) are spindle-shaped, as their name implies. They are longer and narrower than the cells. They establish the transition between the nuclei and cells on the one hand, and the fibro-plastic fibres on the others.

The fibro-plastic fibres are longer and narrower still. We have represented, at the letter *d*, transition forms which mark the connection between the fusiform bodies and fibres.

Lastly, these fibres, when fully developed, juxtapose parallel to their long axis, and give rise to the fibroid structure, (*e.*) which may end subsequently by a transformation into true fibrous tissue.

Such are fibro-plastic elements. There are many tumours in which all of them may be found. Such tumours are of medium density. But it often happens that one or another of the elements predominates. Sometimes the tumour is composed almost exclusively of free nuclei and fibro-plastic cells. It is soft, under these circumstances, and is readily mistaken for encephaloid. When on the other hand, fusiform bodies and fibro-plastic fibres predominate, the tumour is hard, and liable to be confounded with schirrus or fibrous tumour.

III.—*Epithelial or cancroid tumours.*—The elements that compose these tumours are analogous to those which form the epithelium of the skin or mucous membranes.

Setting aside the *nuclear* epithelium of the glandular mucous surfaces, all other epithelia are formed of cellular elements. Epithelial cells exist in three forms: 1. On the skin and many mucous surfaces (mouth, œsophagus, vagina, anus, etc.), the cells appear as thin angular scales, their borders lying in contact, like pieces of mosaic. This is the lamellar, pavement, tessellated, scaly epithelium. In the cylindrical or columnar epithelium, which is found, for example, on the stomach and intestines, the constituent cells are elongated perpendicularly to the mucous membrane on which they are implanted; they form short upright juxtaposed columns. 3. Lastly, the vibratile or ciliated epithelium, which is found chiefly on the air-passages, is simply a cylin-

drical epithelium, the columnar particles of which are terminated by vibrating hair-like processes of *cilia*.

These are the three forms of normal epithelium. The pavement epithelium, which is much the most extensively distributed in the economy, is also the species that constitutes the tissue of the greater number of epithelial tumours.

We find in these tumours irregular polygonal flattened scales (*See* Fig. 3.), which are epithelial cells in different phases of development. There are always a certain number of free nuclei (*a.*), small, and usually irregular; secondly, small irregular cells (*b. c.*), less flat, and less obviously polygonal than the cells of a more advanced stage. The majority of the cells are broad thin scales, presenting, commonly, in some part an indistinct spot, the last vestige of the nucleus. In some cells the nucleus is entirely wanting. The extreme tenuity and flexibility of these cells gives rise to great diversity in their aspects. When we get a front view of the cell, it presents a well defined irregularly polygonal border; it is common to observe two or more superimposed cells, as is represented in the figure; in this case, the transparency of the superficial cell enables us to distinguish readily the angular outline of the subjacent cell. This phenomenon is peculiar to epithelial cells. Other cells are two thick to allow objects beneath them to be seen, unless the focus is varied by turning the large rachet wheel of the microscope. A number of folds always remain on the surface of epithelial cells, however exactly they are laid out; these folds appear as fine and crooked striæ. These are seen on a front view. But many cells present themselves in another point of view. They are curled up, folded on themselves (*d. d.*), and their aspect is then still more characteristic. No other microscopical element presents a similar configuration. Besides the elements we have described, many epithelial tumours contain large rounded bodies, formed by the juxtaposition of several epithelial scales agglomerated around a sort of central nucleus. These are the *epidermic* or *epithelial globes*. We do not dwell upon them, because they are not invariably components of epithelial tumours. We cannot refrain, however, from remarking that, when they do exist, they constitute a most evident and absolutely pathognomonic characteristic of this species of tumour.

IV.—*Cancer.*—Cancerous tumours consist of elements utterly dis-

similar from those we have described. We still have cells and nuclei, but their form, dimensions, and arrangement distinguish them most clearly.

The fundamental and characteristic element is the *cancer nucleus*. The nucleus is sometimes free, sometimes included in a cell wall. Free nuclei are never absent. They occasionally exist alone, constituting *nuclear cancer*. The free nuclei (*a.*) are exactly similar to those contained in cells. They are remarkable for their large size, their uniformity, and the dimensions of their nucleoli. There are commonly only one or two nucleoli in each nucleus; but there may be three.

The diversity of the cells is in striking contrast with the uniformity of the nucleus. Some (*b.*) are small and regular; sometimes they preserve their regularity as they increase (*c.*), but in other cases (*d. g.*), they assume the oddest and most irregular forms. Most of the cells contain only a single nucleus; but not unfrequently two or more nuclei are found in the same cell (*d.*). Lastly, it is not rare to find cells that contain one or more nucleated cells (*e.*); these are called *mother-cells*. This extreme variety in the form of cancer cells has been thought to prove that there was nothing specific in these elements. This is perfectly true. The nucleus alone is specific; but the capricious variations in the cells, far from embarrassing the diagnosis, is one of the best characteristics of cancerous tumours. No other accidental product exhibits such changing forms; besides, the nucleus is always present, to establish the identity of these varied cells.

Apart from these nucleo-cellular elements, cancerous tumours contain accessory elements, to which the diversities in their aspect and consistency are due. The most important of these is fibrous tissue. If this is abundant, the tumour is hard, and takes the name of schirrus; if it is sparingly developed, the tumour is soft, and is termed encephaloid. etc.

These are the anatomical elements that constitute the morbid growths that have been called cancer. It suffices to cast the eye on the figures that delineate them, to lose all desire to confound one with another. We might add to the differences of form we have described, other most important points of difference, arising from the relative dimensions of these dissimilar elements. It may be remarked that the fibro-plastic and cancerous elements are represented in figures 2 and 4, as they appear when observed by the same magnifying power; yet the fibro-plastic nuclei and cells are much smaller than those of cancer. In figure

3, the cells appear of the same size as those of figure 4, but the magnifying power employed was less. (270 : 460, that is, nearly as 3 : 5.)

Thus a microscopical examination reveals in our four groups of so called cancerous tumours, differences in nature, in form, in arrangement, and in the dimensions of their elements. This alone would legitimate a distinction of these tumours. But in addition to this, differences of structure, often glaring, and always appreciable to the naked eye, coincide with these histological diversities, and these various tumours, thus distributed by pathological anatomy into four categories, are distinguished from each other by numerous characteristics derived from their symptoms and progress.